Pericytes contribute to the stability of the vascular network of osteogenic tissue formed from cell sheet-based constructs

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Despite the increased use of cell sheets for tissue engineering, the application of this new technology for thick tissue reconstruction is being limited by old barriers such as the need to create a pre-vascular network to ensure proper nutrient and oxygen supply *in vivo*. In the present work, we created a cell sheet-based construct by co-culturing bone marrow-derived osteogenic and pericyte-like cells with human umbilical vein endothelial cells(HUVECs) with the purpose of enhancing the *in vivo* vascularization of newly formed osteogenic tissue. Human bone marrow mesenchymal stromal cells(hBMSCs) were isolated and cultured in medium supplemented with osteogenic factors or TGF-β1 to obtain either osteogenic or CD146+ pericyte-like cells. Immunocytochemistry analysis of the co-cultures showed organized structures formed by CD146+ hBMSCs and HUVECs over the osteogenic cell sheet, suggesting the existence of cross-talk between the co-cultured cell types. Nude mice were used to test the ability of those constructs to form functional and vascularized osteogenic tissue. Immunohistochemistry analysis of cell sheet-based constructs after 1 and 3 weeks of transplantation revealed the integration of HUVECs with neighboring host's vessels. Additionally, the analysis of the diameter of the blood vessels showed a higher mean diameter for the condition that combined pericyte-like cells and HUVECs, reinforcing the advantage of the proposed model regarding blood vessels maturation and stability.